

**CONCLUSION**

Applicants respectfully request that the amendments and remarks made herein be entered and made of record in the file history of the subject application.

Respectfully submitted,

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Attachments: Exhibits A and B

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**EXHIBIT A**

**MARKED-UP VERSION OF PARAGRAPHS AMENDED IN THE SPECIFICATION**

**(App'n No. ; Attorney Docket No. 9408-042-999)**

**Dated September 18, 2001**

On page 1 of the specification, immediately following the title and before section 1 entitled Field of the Invention, please add the following paragraph reciting the cross-reference to related applications:

This application is the U.S. national phase of International Application No. PCT/US00/06950 filed March 16, 2000, which is a continuation-in-part of U.S. Application No. 09/272,970 filed March 19, 1999, each of which is incorporated-by-reference herein in its entirety.

On page 5, line 37, delete the phrase "the method of claim 4 wherein" such that the paragraph beginning "In another embodiment" from page 5, line 12 to page 6, line 4 reads as follows:

In another embodiment, the invention provides a method for screening a nucleic acid sample from one or more subjects for the presence of a polymorphism comprising the following steps in the order stated: a) contacting the nucleic acid sample in solution with one or more nucleotide polymorphism-specific peptide-labeled oligonucleotide probes under conditions conducive to hybridization of the probes to nucleic acid in the sample; each probe comprising a first and a second marker; such that one or more hybrid molecules are formed between the nucleic acid and one or more nucleotide polymorphism-specific oligonucleotide probes; b) capturing at least one of the one or more hybrid molecules on a solid phase surface; c) contacting the solid phase surface with mung bean nuclease, under conditions wherein the nuclease is active; d) removing material not bound to the solid phase surface; e) contacting the solid phase surface with (i) a first partner molecule with the ability to specifically bind the first marker, and (ii) a second partner molecule with the ability to specifically bind the second marker, said first partner molecule comprising a first detectable label and said second partner molecule comprising a second detectable label that produces a signal distinguishable from the first detectable label; f) removing material not

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bound to the solid phase surface; g) detecting or measuring from the solid phase surface a first signal from the first detectable label and a second signal from the second detectable label; h) cleaving the hybrid molecules on the solid phase surface at mismatched base pairs; and i) detecting or measuring from the solid phase surface a third signal from the detectable label and a fourth signal from the second detectable label, determining a first ratio of the second signal to the first signal, and a second ratio of the fourth signal to the third signal, and comparing the first ratio to the second ratio, wherein a difference between the first ratio and the second ratio indicates that a polymorphism is identified. In one embodiment of these methods the first or second marker is covalently attached to a biotin moiety and the first or second partner molecule is avidin or streptavidin. In another embodiment, [the method of claim 4 wherein] the first or second marker is covalently attached to a carbohydrate moiety and the first or second partner molecule is a lectin. In another embodiment, the first partner molecule is an antibody that binds specifically to the first marker and the second partner molecule is an antibody that binds specifically to the second marker.

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